

In the Claims:

1. (Currently Amended) A method for discriminating dysplastic cells ~~over-expressing~~ INK4a gene products from other non-dysplastic cells expressing INK4a gene products at a detectable level in a biological samples sample comprising determining in a ~~cytological or histological testing procedure~~ the biological sample the co-expression of at least two marker molecules in at least one single cell, wherein at least one marker molecule is an INK4a gene product, which is an expression product encoded by the INK4a gene, and at least one further marker molecule is a cell proliferation marker, wherein the over-expression of the at least one INK4a gene product and expression of the at least one cell proliferation marker for active cell proliferation at a detectable level within said single cell is indicative of the dysplastic state of the cell, and ~~wherein~~ the over-expression of the at least one INK4a gene product and expression of the at least one cell proliferation marker for senescence, terminal cell differentiation, apoptosis or cell cycle arrest at a detectable level within said single cell is indicative of the non-dysplastic state of the cell.
2. (Currently Amended) A The method according to claim 1, wherein a set of two or more cell proliferation markers is detected.
3. (Currently Amended) A The method according to claim 1 ~~or 2~~, wherein ~~at least one the~~ INK4a [[gene-product]] gene product has a molecular weight between 13 and 19 kDa.
4. (Currently Amended) A The method according to ~~claims 1 to 3~~ claim 1, wherein ~~at least one the~~ INK4a [[gene-product]] gene product is selected from a ~~group comprising the~~ group consisting of p16^{INK4a} and p14ARF.
5. (Currently Amended) A The method according to ~~any one of the preceding claims~~ claim 1, wherein ~~at least one the~~ cell proliferation marker is selected from a ~~group comprising the~~ group consisting of a proliferation marker necessary for the maintenance of cell proliferation, a proliferation marker engaged in DNA replication, a proliferation marker being or encoding a member of the processive replication fork, a senescence marker, a cell cycle arrest marker and an apoptosis marker.

6. (Currently Amended) The method according to claim 5, wherein the ~~gene-product~~ proliferation marker necessary for the maintenance of cell proliferation is a molecule selected from a ~~group comprising the group consisting of~~ Ki67 molecules, Ki-S5 molecules and Ki-S2 molecules.
7. (Currently Amended) The method according to claim 6, wherein the ~~gene-product~~ proliferation marker engaged in DNA replication is selected from a ~~group comprising the group consisting of~~ helicases or subunits thereof, cell division cycle (~~ede~~) molecules, phosphatase molecules and kinase molecules.
8. (Currently Amended) The method according to claim 7, wherein the helicases or subunits thereof are selected from a ~~group comprising the group consisting of~~ MCM2, MCM3, MCM4, MCM5, MCM6, MCM7 and HELAD1.
9. (Currently Amended) The method according to claim 7, wherein the ~~ede~~ cell division cycle molecules, kinases molecules and phosphatases molecules are selected from a ~~group comprising the group consisting of~~ CDC6, CDC7 protein kinase, Dbf4, CDC14 protein phosphatase, CDC45 and MCM10.
10. (Currently Amended) The method according to claim 5, wherein the ~~molecules engaged in member of~~ the processive replication fork is selected from a ~~group comprising the group consisting of~~ PCNA and POLD.
11. (Currently Amended) A ~~The method according to any one of the claims 1-10~~ claim 1, wherein the ~~gene-product~~ INK4a gene product is a polypeptide or a nucleic acid molecule.
12. (Currently Amended) A ~~The method according to any one of the preceding claims~~ claim 1, wherein additionally at least one further marker molecule is detected for improvement of the assessment of diagnosis or prognosis.
13. (Currently Amended) A ~~The method according to claim 12~~, wherein the further marker molecule is at least one further proliferation marker molecule.

14. (Currently Amended) A The method according to claim 12 ~~or 13~~, wherein the further marker molecule is selected from ~~a group comprising the group consisting of~~ a senescence marker, an apoptosis marker, a cell cycle arrest marker, a marker for terminal differentiation of cells, a marker for viral infection, a marker for viral activity, a cell cycle regulatory protein, a gene-product necessary for the maintenance of cell proliferation, a gene-product engaged in DNA replication, and a ~~[[gene-product]]~~ gene product being a member of the processive replication fork.
15. (Currently Amended) A The method according to ~~any one of the preceding claims claim~~ 12, wherein additionally a cytological staining procedure employing at least one dye selected from ~~a group comprising the group consisting of~~ DAPI, Quinacrin, Chromomycin, Azan, Acridin-orange, Hematoxylin, Eosin, Sudan-red, Toluidin-blue, and Thionin, or a staining method selected from ~~a group comprising the group consisting of~~ Pap-staining, Giemsa-staining, Hematoxylin-Eosin staining, van-Gieson-staining, Schiff-staining, staining via metal precipitates, Turnbolls-blue-staining and staining via metal cyanides, is applied.
16. (Currently Amended) The method according to ~~any one of the preceding claims claim~~ 1, wherein the dysplastic cells are cells of a cancerous or precancerous lesion.
17. (Original) The method according to claim 16, wherein the dysplastic cells are cells of a dysplasia being associated with a papilloma virus.
18. (Currently Amended) The method according to claim 17, wherein the papilloma virus is a high risk human papilloma virus selected from ~~a group comprising the group consisting of~~ HPV16, HPV18, HPV31, HPV 33, HPV35, HPV 39, HPV 45, HPV 51, HPV 52, HPV56, HPV 58, HPV 59, HPV 66 and HPV 68.
19. (Currently Amended) The method according to ~~any one of the claims 16 to 18 claim~~ 16, wherein the lesion is selected from ~~a group comprising the group consisting of~~ a lesion of the anogenital tract, a lesion of the respiratory tract and a lesion of the skin and it's appendages.
20. (Currently Amended) The method according to claim ~~17 or~~ 19, wherein the lesion is

selected from ~~a group comprising~~ the group consisting of a lesion of the uterine cervix, a lesion of the vagina, a lesion of the vulva, a lesion of the penis, a lesion of the anus, a lesion of the rectum, a lesion of the bronchic tree, a lesion of the lung, a lesion of the peritoneal space, a lesion of the naso-pharyngeal space, a lesion of the oral cavity ~~or~~ and a lesion of the skin.

21. (Currently Amended) A The method according to ~~any preceding claim~~ claim 1, wherein the biological sample is a sample containing cells originating from the anogenital tract, from the respiratory tract or from the skin and its appendages.
22. (Currently Amended) A The method according to claim 21, wherein the ~~cells are cells~~ originating biological sample is obtained from the uterine cervix, the vagina, the vulva, the penis, the anus, the rectum, the bronchic tree, the lung, the naso-pharyngeal space, the oral cavity or the skin.
23. (Currently Amended) A The method according to ~~any one of the preceding claims~~ claim 22, wherein the biological sample is a cytological or histological preparation.
24. (Currently Amended) A The method according to ~~any one of the preceding claims~~ claim 1, wherein the ~~detection~~ determination of the INK4a ~~[[gene-products]]~~ gene product and/or the cell proliferation marker molecules is performed using at least one probe specifically recognising at least one of the respective molecules to be detected.
25. (Currently Amended) A The method according to claim 24, wherein the at least one probe is detectably labelled with at least one label.
26. (Currently Amended) A The method according to claim 25, wherein ~~at least one~~ the label is selected from the group consisting of a radioisotope, a bioluminescent compound, a chemiluminescent compound, a fluorescent compound, a metal chelate, ~~or~~ and an enzyme.
27. (Currently Amended) A The method according to ~~any one of the claims 24 to 26~~ claim 24, wherein ~~at least one~~ the probe is a protein and/or a nucleic acid.
28. (Currently Amended) A The method according to claim 27, wherein ~~at least one probe~~ the protein is an antibody directed against a INK4a encoded ~~[[gene-products]]~~ gene product

or a cell proliferation marker gene product.

29. (Original) The method according to claim 28, which comprises an immuno-cytochemical staining procedure.
30. (Currently Amended) The method according to claim 25 ~~or 26~~, wherein ~~at least one~~ the probe is a nucleic acid specifically hybridizing to an INK4a [[gene-product]] gene product or a cell proliferation marker gene product.
31. (Original) The method according to claim 30, which comprises an in situ hybridization reaction.
32. (Original) The method according to claim 30, which comprises a nucleic acid amplification reaction.
33. (Original) The method according to claim 32, wherein the nucleic acid amplification reaction is PCR, NASBA or LCR.
34. (Currently Amended) ~~A~~ The method according to ~~any of the preceding claims~~ claim 27, wherein ~~detection reactions~~ the determination using nucleic acid probes and polypeptide probes are carried out simultaneously.
35. (Currently Amended) ~~A kit for performing the method according to any one of the preceding claims, which is a diagnostic kit or a research kit,~~ comprising at least one or more probes for the detection of the presence or absence and/or the level of the over-expression of at least one INK4a [[gene-product]] gene product and at least one cell proliferation marker gene product in biological samples.
36. (Currently Amended) ~~A~~ The kit according to claim 35, wherein the INK4a gene products are selected from ~~a group comprising the group consisting of~~ p16^{INK4a} and p14ARF.
37. (Currently Amended) ~~A~~ The kit according to claim 35 ~~or 36~~, wherein the cell proliferation marker gene products are selected from ~~a group comprising the group consisting of~~ CDC6, MCM3, MCM3, MCM4, MCM5, MCM6, MCM7, CDC7 protein kinase, Dbf4, CDC14 protein phosphatase, CDC45 and MCM10, Ki67, Ki-S2, PCNA ~~or~~ and POLD.

38. (Currently Amended) The kit according to ~~claims 35 to 37~~ claim 35 furthermore comprising at least one of the following:

- a. a p16^{INK4a} sample for carrying out a positive control reaction,
- b. a p14ARF sample for carrying out a positive control reaction,
- c. a Ki67 sample for carrying out a positive control reaction,
- d. a Ki-S2 sample for carrying out a positive control reaction,
- e. an MCM5 sample for carrying out a positive control reaction,
- f. an MCM2 sample for carrying out a positive control reaction,
- g. a PCNA sample for carrying out a positive control reaction,
- h. reagents for detection of the presence or absence and/or the level of p16INK4a,
- i. reagents for detection of the presence or absence and/or the level of p14ARF,
- j. reagents for detection of the presence or absence and/or the level of Ki67,
- k. reagents for detection of the presence or absence and/or the level of Ki-S2,
- l. reagents for detection of the presence or absence and/or the level of MCM5,
- m. reagents for detection of the presence or absence and/or the level of MCM2,
- n. reagents for detection of the presence or absence and/or the level of PCNA,
- o. one or more samples of INK4a gene-products for carrying out positive control reactions,
- p. one or more samples of cell proliferation marker gene-products for carrying out positive control reactions,
- q. one or more reagents for the detection of the presence or absence and/or the level of other INK4a gene products, or
- r. and one or more reagents for the detection of the presence or absence and/or the level of other cell proliferation marker gene products.